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EVALUATION OF PERFUSION INDEX AS A PREDICTOR OF VASOPRESSOR REQUIREMENT IN PATIENTS WITH SEVERE SEPSIS

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ABSTRACT—We evaluated the ability of perfusion index (PI) to predict vasopressor requirement during early resuscitation in patients with severe sepsis. All consecutive patients with clinically suspected severe sepsis as defined by the criteria of the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference were included. Perfusion variables included PI, arterial lactate level, central venous oxygen saturation, and the difference between central venous carbon dioxide and arterial carbon dioxide pressures, and were recorded before resuscitation and 6 h thereafter. We enrolled 36 patients with severe sepsis. Twenty-one patients required vasopressors, whereas 15 did not. The cut-off of the PI value for predicting vasopressor requirement was $\leq$0.3. This cut-off value had a sensitivity of 100% and a specificity of 93%; the area under the curve was 0.96 (95% confidence interval 0.8–0.99, $P < 0.0001$). The cut-off of the arterial lactate level for predicting vasopressor requirement was $\geq 1.8\,mg\,dL^{-1}$. This cut-off value had a sensitivity of 82% and a specificity of 80%; the area under the curve was 0.84 (95% confidence interval 0.68–0.94, $P < 0.0001$). Other perfusion variables failed to predict vasopressor requirement in patients with severe sepsis. We concluded that PI and arterial lactate level are good predictors of vasopressor requirement during early resuscitation in patients with severe sepsis. Further studies are warranted to investigate whether monitoring PI during resuscitation improves the outcome of patients with septic shock.

KEYWORDS—Central venous oxygen saturation, lactate, mortality, perfusion index, severe sepsis, venous–arterial carbon dioxide pressure difference

INTRODUCTION

Despite many campaigns and evidence-based recommendations for its management, septic shock remains the leading cause of death worldwide, with in-hospital and intensive care mortality rates of 11.9% to 47.2%, depending on the setting and severity of the disease (1).

The high mortality rate of sepsis is related to the quality of management and complex nature of the disease. The loss of autoregulation, and altered regional and microvascular blood flow characteristic of septic shock jeopardize both central and peripheral tissue perfusion (2–4). Although the relationship between the systemic and peripheral circulation in patients with sepsis is poorly understood, the persistent impedance of peripheral tissue perfusion is associated with high mortality in these patients (5). Consequently, methods of monitoring peripheral tissue perfusion in these patients are in demand. Perfusion index (PI) is a reliable indicator of peripheral perfusion derived from the photoelectric plethysmographic signal of a pulse oximeter (6). PI is the ratio between the pulsatile and nonpulsatile portions of the plethysmographic waveform. The pulsatile portion decreases with vasoconstriction and increases with vasodilatation; thus, changes in PI reflect changes in peripheral vasomotor tone (7).

According to the current treatment guidelines, vasopressor therapy should be initiated within 6 h of the diagnosis of sepsis to maintain tissue perfusion if patients remain hypotensive despite adequate fluid resuscitation (8). More recently, a retrospective study (9) identified a strong association between the early initiation of vasopressor therapy and reduced mortality in these patients. These findings raise an important question: can the requirement for vasopressor therapy be predicted in patients with severe sepsis?

We conducted a prospective observational study to examine whether PI can predict vasopressor requirement during early resuscitation in patients with severe sepsis.

MATERIALS AND METHODS

This prospective observational study was conducted in the 24-bed trauma–surgical intensive care unit (ICU) at Cairo University Hospital, Giza, Egypt. The study protocol was approved by the Research Ethics Committee, and informed consent was obtained from patients' next-of-kin before commencement. All patients with clinically suspected severe sepsis, as defined by the criteria of the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference, were consecutively included between June 2014 and January 2015 (10). Patients aged under 18 years, who were pregnant or who were already receiving vasopressor/inotropic drug therapy at ICU admission, were excluded. Seventy patients were admitted to the ICU during this period; of which, 34 cases were excluded for various reasons: 25 patients were receiving vasopressor at ICU admission, and 9 patients did not consent.

Study protocol

All participants received broad-spectrum antibiotic therapy. Temperature, noninvasive and invasive arterial blood pressure, five-lead electrocardiography, hourly urinary output, and central venous pressure (CVP) were monitored in all patients. Upon ICU admission, patients were resuscitated to achieve early goal-directed therapy, as recommended by the Surviving Sepsis Campaign: CVP was maintained at 8–12 mm Hg; mean arterial pressure (MAP) at $\geq$65 mm Hg; and central venous oxygen saturation ($ScvO_2$) at $\geq$70%. Initially, all patients received $30\,mL\,kg^{-1}$ crystalloid fluid over 1 h. Fluid administration was continued (isotonic crystalloid fluid) until CVP reached 8–12 mm Hg. In mechanically ventilated patients, fluid therapy was continued until pulse pressure variation dropped below 13%.

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PPV was measured through a Philips Intellivue MP 70 monitor (Philips, Suresnes, France). If MAP remained <65 mm Hg after administration of the initial fluid bolus, norepinephrine infusion was titrated to maintain MAP ≥65 mm Hg. The intensivists were blinded for the results of the PI and arterial lactate.

Data collection

Hemodynamic, metabolic, and PI variables—heart rate (HR), MAP, CVP, and temperature—were recorded. Simultaneous blood gas measurements were obtained from arterial and central venous catheters. Blood gas analysis was performed, and arterial lactate concentration was determined using the GEM Premier 3000 (Instrumentation Laboratory, Bedford, MA). $ScvO_2$ was calculated from a sample taken from the central venous catheter, the tip of which was confirmed to be in the superior vena cava near or at the right atrium by radiography. The central venous–arterial blood carbon dioxide partial pressure difference ($Pv-aCO_2$) was calculated as the difference between the partial pressures of central venous carbon dioxide ($PcvCO_2$) and arterial carbon dioxide ($PaCO_2$). PI and the percentage pulse oxygen saturation were measured by attaching a pulse oximeter probe (Masimo Radical 7; Masimo Corp., Irvine, CA) to the left index finger. The readings were recorded after signal stabilization. All aforementioned variables were recorded 5 min after initial fluid resuscitation (30 mL kg^{-1}) (T0) and 6 h thereafter (T6). The use of vasopressors was defined as any administration of vasopressor medication within 24 h of ICU admission after initial fluid resuscitation.

We also collected data on patient characteristics, including age and sex; source of infection; hemoglobin concentration; liver function (as indicated by aspartate aminotransferase [AST] and alanine aminotransferase [ALT] levels, and international normalized ratio [INR]); and renal function (urea and creatinine levels). The severity of the disease and organ failure were quantified using Acute Physiology and Chronic Health Evaluation (APACHE) II (11) and Sequential Organ Failure Assessment (SOFA) (12) scores, respectively. Survival was monitored for 28 days.

Statistical analysis

Data are expressed as means (with standard deviation) unless specified otherwise and were compared as follows: continuous variables with the Mann-Whitney *U* test; and categorical variables with the chi-square test. Paired variables within each group were compared with a Wilcoxon matched-pairs test. To compare the performance of PI, lactate, $Pv-aCO_2$, and $ScVO_2$ in predicting vasopressor requirement and/or mortality, receiver-operating characteristic (ROC) curves were constructed and the area under the curve (AUC) was calculated. MedCalc version 12.1.4.0 (MedCalc Software bvba, Mariakerke, Belgium) generated perfusion values with the highest sensitivity and specificity (Youden index). The AUC of the ROC curves were compared using a Hanley-McNeil test. The level of significance was set at $P < 0.05$ for two-tailed tests. Statistical analysis was performed using SPSS for Windows version 15.0 (SPSS Inc., Chicago, IL).

RESULTS

We enrolled 36 patients who fulfilled the inclusion criteria, 15 of whom died and 21 survived. Twenty-one (58.3%) patients required vasopressors, whereas 15 did not. Baseline demographic, physiological, and laboratory data, and severity scores are shown in Table 1. All patients except two needed mechanical ventilation. The most frequent source of sepsis was abdominal infection (22, 61%), followed by soft tissue infection (12, 33.5%) and pneumonia (2, 5.5%). APACHE II scores and white blood cell counts did not significantly differ between patients who required vasopressors and those who did not. However, SOFA scores were significantly higher in the vasopressor group than in the nonvasopressor group ($P = 0.009$). There were no significant differences in other laboratory data (ALT, AST, urea, and creatinine) between the two study groups except for INR, which was significantly higher in the vasopressor group compared with the nonvasopressor group ($P = 0.01$).

Hemodynamic and perfusion variables

The evolution of hemodynamic, peripheral, and central perfusion parameters at T0 and T6 are shown in Tables 2 and 3. PI was successfully evaluated in all patients in the study. HR, respiratory rate, temperature, and CVP were comparable between the study groups. Mean arterial pressure was significantly higher at baseline in the nonvasopressor group compared to the other group. There were no significant differences in $ScVO_2$, SaO_2, PaO_2, $PaCO_2$, $PvCO_2$, and $Pv-aCO_2$ between patients who required vasopressors and those who did not. In contrast, baseline arterial lactate level at T0 was significantly higher in the vasopressor group than in the nonvasopressor group (4.5 [3.4] vs. 1.7 [1.1] mmoL L^{-1}, $P < 0.0001$), whereas PI was significantly lower in patients who required vasopressors than patients who did not (0.17 [0.08] vs. 1.4 [1.2], $P < 0.0001$; Table 3). From T0 to T6, decreases in both PI and arterial lactate levels were significantly greater in patients who required vasopressors than in those who did not. Relative

TABLE 1. **Patient characteristics**

Variables	All patients (n = 36)	Vasopressors (n = 21)	No vasopressors (n = 15)	*P*
Age (years)	50 (17.9)	54 (16.5)	45 (19)	0.2
Sex (M/F)	21/15	11/10	10/5	0.39
APACHE II score	21 (11)	21 (6)	20 (16)	0.08
SOFA score	4 (2.6)	5 (2)*	3 (2)	0.009
GCS	14 (14–15)	14 (14–14.5)	15 (14–15)	0.015
Source of infection				0.4
Abdominal infection	22 (61%)	10 (66.7%)	12 (57.1 %)	
Soft tissue infection	12 (33.3%)	5 (33.3%)	7 (33.3%)	
Pneumonia	2 (5.6%)	0	2 (9.5%)	
WBCs	20 (13)	21.6 (15.5)	17.5 (10)	0.6
Hemoglobin (g dL^{-1})	10 (8.5–12.5)	10.3 (8.6–13)	9.0 (8.5–11)	0.27
Urea (mg dL^{-1})	96 (55–135)	97 (55–171)	96 (22–125)	0.4
Creatinine (mg dL^{-1})	1.5 (1.1–3.1)	1.4 (1.2–3.1)	1.9 (1.1–2.6)	0.7
ALT (IU L^{-1})	27 (19–52)	30 (19–54)	23 (19–50)	0.8
AST (IU L^{-1})	41 (25–111)	43 (26–141)	32 (21–111)	0.3
INR	1.5 (1.2–1.9)	1.7 (1.4–2)*	1.3 (1.2–1.7)	0.01

ALT, alanine aminotransferase; APACHE, Acute Physiology and Chronic Health Evaluation; AST, aspartate aminotransferase; GCS, Glasgow Coma Score; INR, international normalized ratio; SOFA, Sequential Organ Failure Assessment. Data are presented as means (standard deviation), medians (interquartile ranges), or numbers (percentages).
*Statistically significant ($P < 0.05$).

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Table 2. **Hemodynamic and perfusion variables in the study groups before vasopressor and after volume resuscitation**

Variables	Vasopressors (n = 21)	No vasopressors (n = 15)	*P*
Heart rate (beats min^{-1})	120 (102–134)	105 (100–123)	0.14
MAP (mm Hg)	63 (55–66)	80 (69–95)	0.002
Respiratory rate	35 (23–40)	27 (24–30)	0.4
Temperature (°C)	38.5 (36.7–39)	38.5 (37–39)	0.8
CVP (mm Hg)	9 (8–9.5)	9 (7–11)	0.7
PI	0.17 (0.08)*	1.4 (1.2)	< 0.0001
Lactate	4.5 (3.4)*	1.7 (1.1)	< 0.0001
$ScVO_2$	62 (13)	67 (12)	0.26
SaO_2	96.7 (3)	97.6 (2.6)	0.32
PaO_2	141 (90)	138 (84)	0.8
$PaCO_2$	32 (9.2)	26 (8)	0.3
$PvCO_2$	36 (10)	33 (7)	0.35
$Pv–aCO_2$	4.5 (4.7)	6.8 (5)	0.07

CVP, central venous pressure; MAP, mean arterial pressure; PaO_2, arterial oxygen tension; $PaCO_2$, arterial carbon dioxide tension; PI, perfusion index; $Pv–aCO_2$ gap, venous to arterial carbon dioxide difference; $PvCO_2$, venous carbon dioxide tension; SaO_2, arterial oxygen saturation; $ScVO_2$, central venous oxygen saturation. Data are presented as medians (interquartile ranges).
*Denotes statistical significance ($P < 0.05$).

to the baseline (T0), PI was significantly lower at T6 in the vasopressor group, whereas it did not change significantly in the nonvasopressor group.

Central and peripheral perfusion variables as predictors of vasopressor requirement

The cut-off value, sensitivity, specificity, and AUC of the ROC curves for the variables examined are shown in Table 4. PI and arterial lactate level were the only perfusion variables able to predict vasopressor requirement during initial resuscitation. The optimum cut-off value of PI for predicting vasopressor requirement according to the maximum Youden index was ≤ 0.3. This cut-off value had a sensitivity of 100% and a specificity of 93%; the AUC was 0.96 (95% confidence interval [CI] 0.8–0.99, $P < 0.0001$). The cut-off value of arterial lactate level for predicting vasopressor requirement was $\geq 1.8\ mg\ dL^{-1}$, with a sensitivity of 82% and a specificity of 80%; the AUC was 0.84 (95% CI 0.68–0.94, $P < 0.0001$). No other perfusion variables ($ScVO_2$ and $Pv–aCO_2$) were able to discriminate between the study groups (Table 4, Fig. 1).

Central and peripheral perfusion variables as predictors of 28-day mortality

The 28-day mortality rate of the 36 septic patients was 40.5% (15 patients). PI, arterial lactate level, and $Pv–aCO_2$ were able to predict mortality with varying sensitivity and specificity. The cut-off of the PI value for predicting 28-day mortality was ≤ 0.21, with a sensitivity of 86% and a specificity of 90% (AUC 0.94 [95% CI 0.8–0.99, $P < 0.0001$]). The cut-off of the arterial lactate level for predicting mortality was ≥ 2.1, with a sensitivity of 86% and a specificity of 71% (AUC 0.82 [95% CI 0.65–0.92, $P < 0.0001$]). Both PI and arterial lactate level were significantly better than $Pv–aCO_2$ at predicting 28-day mortality (Table 5). The cut-off value of $Pv–aCO_2$ for predicting mortality was ≥ 6, with a sensitivity of 80% and a specificity of 62% (AUC 0.73 [95% CI 0.56–0.87, $P = 0.005$]). Both $ScVO_2$ and MAP performed poorly in predicting 28-day mortality. The ROC curves of baseline PI, arterial lactate level, $Pv–aCO_2$, $ScVO_2$, and MAP for predicting 28-day mortality in patients with sepsis are shown in Figs. 2 and 3.

Table 3. **Hemodynamic and perfusion variables in the study groups 6 h after resuscitation**

Variables	Vasopressors (n = 21)	No vasopressors (n = 15)	*P*
Heart rate (beats min^{-1})	110 (86–127)	100 (95–110)	0.2
MAP (mm Hg)	78 (64–87)	84 (78–98)	0.2
Respiratory rate	35 (23–40)	27 (24–30)	0.4
Temperature (°C)	37 (36–38.4)	38 (37–38)	0.8
CVP (mm Hg)	10 (8–12)	12 (8–14)	0.18
PI	0.07 (0.01–0.27)*,†	0.8 (0.5–1)	<0.0001
Lactate	1.9 (1.1–4.1)*,†	1.15 (0.7–1.9)	<0.0001
$ScVO_2$	54 (27)	68 (10)	0.19
SaO_2	98.7 (1.4)	96.6 (1.9)	0.7
PaO_2	126 (90)	117 (84)	0.7
$PaCO_2$	28 (15)	30 (8)	0.5
$PvCO_2$	34 (17)	35 (11)	0.35
$Pv–aCO_2$	6 (7.5)	4.6 (5.3)	0.6

CVP, central venous pressure; MAP, mean arterial pressure; PaO_2, arterial oxygen tension; $PaCO_2$, arterial carbon dioxide tension; PI, perfusion index; $Pv–aCO_2$ gap, venous to arterial carbon dioxide difference; $PvCO_2$, venous carbon dioxide tension; SaO_2, arterial oxygen saturation; $ScVO_2$, central venous oxygen saturation. Data are presented as medians (interquartile ranges).
*Denotes statistical significance compared to other group ($P < 0.05$).
†Denotes significant compared to baseline ($P < 0.05$).

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TABLE 4. **Comparison of the ability of the area under the receiver operating characteristic curves to predict the need for vasopressors**

	AUC of ROC curve	95% CI	Cut-off value	Sensitivity (%)	Specificity (%)	LR (+)	LR (−)	*P*
PI	0.96*	0.83–0.99	0.3	100	93	15	0.00	<0.0001
Lactate	0.84*	0.68–0.94	1.8	82	80	4	0.24	<0.0001
$Pv–aCO_2$	0.67	0.49–0.8	6	71	66	2.1	0.4	0.07
$ScVO_2$	0.61	0.43–0.76	81	95	26	1.3	0.18	0.24

AUC, area under the curve; CI, confidence interval; LR, likelihood ratio; PI, perfusion index; $Pv–aCO_2$, venous to arterial carbon dioxide difference; ROC, receiver-operating characteristic; $ScVO_2$, central venous oxygen saturation.
*Denotes statistical significance ($P < 0.05$).

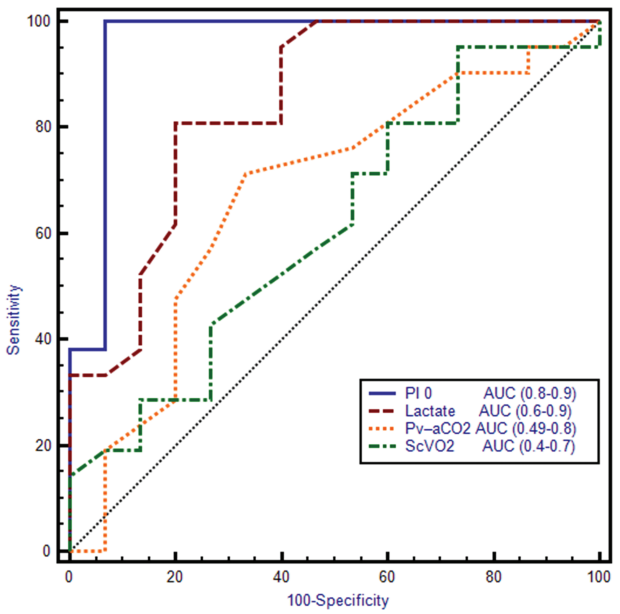

FIG. 1. Receiver-operating characteristic curves comparing the ability of perfusion index, lactate, the difference between central venous carbon dioxide and arterial carbon dioxide pressures, and central venous oxygen saturation to predict the need for vasopressors in patients with severe sepsis. PI, perfusion index; $ScVO_2$, central venous oxygen saturation.

DISCUSSION

The main finding of this study is that low PI is a good indicator of vasopressor requirement in patients with severe sepsis. To the best of our knowledge, this is the first study to evaluate the ability of PI to predict vasopressor requirement during early resuscitation in patients with sepsis.

We found that a PI of ≤0.3 during early resuscitation in patients with sepsis has a sensitivity of 100% and a specificity of 93% for predicting the use of vasopressors in these patients. PI represents the ratio between changes in the pulsatile component of arterial blood volume and changes in the nonpulsatile components of arterial and venous blood volume. These changes are generated by variations in the tone of muscles of the arterial and venous walls under various conditions (7). Under the condition of reduced systemic blood flow, as in patients with septic shock, the sympathetic nervous system is activated and induces vasoconstriction in the cutaneous vascular bed to preserve blood flow to vital organs (13). When peripheral hypoperfusion exists, the pulsatile component of PI decreases, whereas the nonpulsatile component remains unchanged, which may lead to the lower PI value evident in these patients (6). A decrease in PI after vasopressor infusion reflected a more decrease in pulsatile component of PI as a result of increase of vascular tone. The relationship between a sympathetic nervous system-induced increase in vascular tone and decrease of PI value has not been previously described. However, several studies have shown that PI is a sensitive indicator of the development of sympathectomy following either spinal or epidural anesthesia (14, 15).

Another important predictor of vasopressor requirement in patients with sepsis is arterial lactate level. Our data suggest that an arterial lactate level of $\geq 1.8\,mmol\,L^{-1}$ had an 82% sensitivity and an 80% specificity for predicting vasopressor requirement in patients with sepsis. Lactate is commonly used as a marker of tissue hypoperfusion in patients with severe sepsis and septic shock (16); however, there is a paucity of data linking lactate level with the use of vasopressors in these patients. Several studies (17, 18) found that about one-third to one-half of patients with vasopressor-dependent septic shock did not express lactate on presentation and that lactate remained below $2.0\,mmol\,L^{-1}$. More recently, Singer et al. (19) demonstrated that a lactate level of $\geq 2\,mmol\,L^{-1}$ is associated with an increased need for vasopressors (odds ratio [OR] 1.54, 95% CI 1.13–2.12).

Neither $ScVO_2$ nor $Pv–aCO_2$ was able to predict vasopressor requirement in patients with sepsis, suggesting that PI is superior to central perfusion parameters in this regard. In fact, there are few recommendations in the literature on how to predict the use of vasopressors in patients with sepsis. One study (20) used shock index (defined as HR divided by the systolic blood pressure) as a

TABLE 5. **Comparison of the ability of the area under the receiving operating characteristic curves to predict 28-day mortality**

	AUC of ROC curve	95% CI	Cut-off value	Sensitivity (%)	Specificity (%)	LR (+)	LR (−)	*P*
PI	0.94*	0.8–0.99	0.21	86	90	9.1	0.15	<0.0001
Lactate	0.82*	0.65–0.92	2.1	86	71	3	0.19	<0.0001
$Pv–aCO_2$	0.73*	0.56–0.87	6	80	62	2.1	0.32	0.005
$ScVO_2$	0.525	0.35–0.69	50%	26	95	5.6	0.7	0.8

AUC, area under the curve; CI, confidence interval; LR, likelihood ratio; PI, perfusion index; $Pv–aCO_2$, venous to arterial carbon dioxide difference; ROC, receiver-operating characteristic; $ScVO_2$, central venous oxygen saturation.
*Denotes statistical significance ($P < 0.05$).

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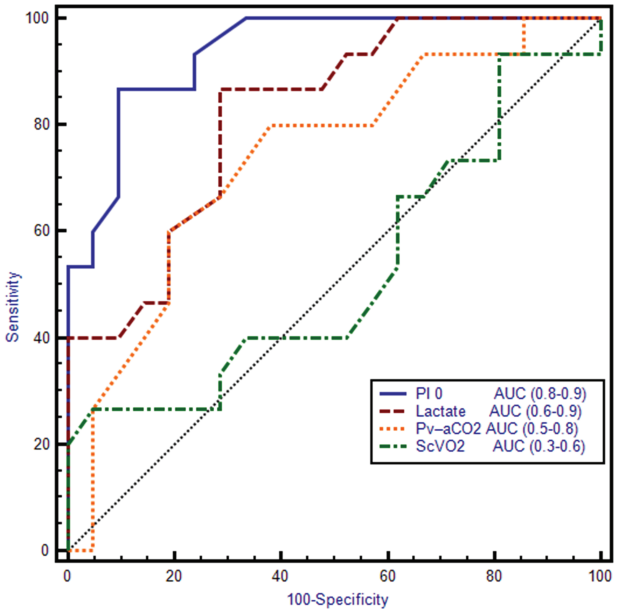

Fig. 2. Receiver-operating characteristic curves comparing the ability of perfusion index, lactate, the difference between central venous carbon dioxide and arterial carbon dioxide pressures, and central venous oxygen saturation to predict 28-day mortality in patients with severe sepsis. PI, perfusion index; $ScVO_2$, central venous oxygen saturation.

predictor of vasopressor use in patients admitted to the emergency department. They found that sustained elevation and not a single value of shock index are good predictors of vasopressor requirement in patients with severe sepsis.

The prediction of vasopressor requirement is critical for determining the optimal timing of the initiation of vasopressor therapy. The importance of timing vasopressor therapy appropriately was recently emphasized in a report on the protocolized management of septic shock (9). Bai et al. (9) analyzed 213 patients admitted to the ICU and found a strong relationship between delayed initial noradrenaline administration and 28-day mortality.

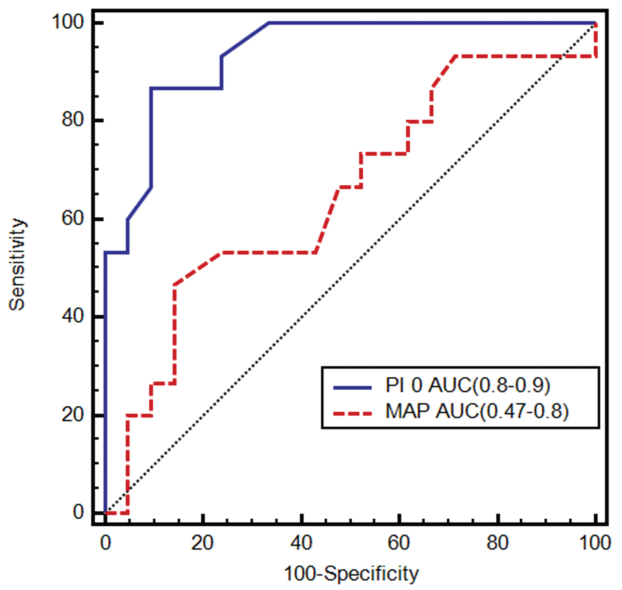

Fig. 3. Receiver-operating characteristic curves comparing the ability of perfusion index and mean arterial pressure to predict 28-day mortality in patients with severe sepsis. MAP, mean arterial pressure; PI, perfusion index.

In this study, PI and arterial lactate level were more powerful predictors of ICU mortality than central perfusion parameters in patients with sepsis. PI has a cut-off value of <0.2 for predicting ICU mortality, which is similar to that previously shown by He et al. (21). They demonstrated that a PI of ≤ 0.2 during early resuscitation in septic patients had a sensitivity of 65% and a specificity of 92% for predicting ICU mortality.

In the present study, $ScVO_2$ performed poorly in predicting ICU mortality. Consistent with our finding, Chung et al. (22) found that mortality of patients with severe sepsis or septic shock was not related to postresuscitation $ScVO_2$ levels.

When selecting a tool for specific diagnostic and/or therapeutic purposes, it is necessary to consider the balance between efficacy and applicability in terms of cost, availability, and invasiveness. PI is a valid, noninvasive, and cheap monitoring method suitable for routine use in the resuscitation of patients with septic shock, with the potential to enhance existing methods of risk stratification in these patients.

Our study had several limitations. First, we did not measure hemodynamic variables such as cardiac output and systemic vascular resistance. However, one study (6) showed that there is no correlation between changes in cardiac output and PI, because of heterogeneity in skin blood flow regulation during changes in global blood flow and associated sympathetic nerve activity. Second, PI is overly sensitive to extraneous factors such as ambient temperature and stress and anxiety, which activate the sympathetic nervous system and induce peripheral vasoconstriction (23, 24). To minimize these factors, PI was recorded under the same ambient temperature and before the administration of any type of sedative or narcotic medication. Finally, although the findings of this study appear promising, they are based on a small number of patients and must be confirmed by a large multicentre study.

In conclusion, a PI of ≤ 0.3 is predictive of vasopressor requirement during early resuscitation in patients with severe sepsis and septic shock. A further randomized controlled study is warranted to investigate whether monitoring PI during septic shock resuscitation influences the time of initiation of vasopressor therapy, with a subsequent improvement in tissue perfusion.

REFERENCES

1. Vincent JL, Marshall JC, Namendys-Silva SA, François B, Martin-Loeches I, Lipman J, Reinhart K, Antonelli M, Pickkers P, Njimi H, et al.: Assessment of the worldwide burden of critical illness: the Intensive Care Over Nations (ICON) audit. *Lancet Respir Med* 2:380–386, 2014.
2. Terborg C, Schummer W, Albrecht M, Reinhart K, Weiller C, Röther J: Dysfunction of vasomotor reactivity in severe sepsis and septic shock. *Intensive Care Med* 27:1231–1234, 2001.
3. Trzeciak S, Dellinger RP, Parrillo JE, Guglielmi M, Bajaj J, Abate NL, Arnold RC, Colilla S, Zanotti S, Hollenberg SM; Microcirculatory Alterations in Resuscitation and Shock Investigators: Early microcirculatory perfusion derangements in patients with severe sepsis and septic shock: relationship to hemodynamics, oxygen transport, and survival. *Ann Emerg Med* 49:88–98, 98.e1-2, 2007.

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4. Poeze M, Solberg BCJ, Greve JWM, Ramsay G: Monitoring global volume-related hemodynamic or regional variables after initial resuscitation: what is a better predictor of outcome in critically ill septic patients? *Crit Care Med* 33:2494–2500, 2005.
5. Lima A, van Bommel J, Jansen TC, Ince C, Bakker J: Low tissue oxygen saturation at the end of early goal-directed therapy is associated with worse outcome in critically ill patients. *Crit Care* 13:S13, 2009.
6. Pinto Lima A, Beelen P, Bakker J: Use of a peripheral perfusion index derived from the pulse oximetry signal as a noninvasive indicator of perfusion. *Crit Care Med* 30:1210–1213, 2002.
7. Hales JR, Stephens FR, Fawcett AA, Daniel K, Sheahan J, Westerman RA, James SB: Observations on a new non-invasive monitor of skin blood flow. *Clin Exp Pharmacol Physiol* 16:403–415, 1989.
8. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, Sevransky JE, Sprung CL, Douglas IS, Jaeschke R, et al.: Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med* 41:580–637, 2013.
9. Bai X, Yu W, Ji W, Lin Z, Tan S, Duan K, Dong Y, Xu L, Li N: Early versus delayed administration of norepinephrine in patients with septic shock. *Crit Care* 18:532, 2014.
10. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, Cohen J, Opal SM, Vincent JL, Ramsay G, et al.: 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med* 31:1250–1256, 2003.
11. Knaus WA, Draper EA, Wagner DP, Zimmerman JE: APACHE II: a severity of disease classification system. *Crit Care Med* 13:818–829, 1985.
12. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, Reinhart CK, Suter PM, Thijs LG: The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med* 22:707–710, 1996.
13. Bond RF: A review of the skin and muscle hemodynamics during hemorrhagic hypotension and shock. *Adv Shock Res* 8:53–70, 1982.
14. Toyama S, Kakumoto M, Morioka M, Matsuoka K, Omatsu H, Tagaito Y, Numai T, Shimoyama M: Perfusion index derived from a pulse oximeter can predict the incidence of hypotension during spinal anaesthesia for Caesarean delivery. *Br J Anaesth* 111:235–241, 2013.
15. Ginosar Y, Weiniger CF, Meroz Y, Kurz V, Bdolah-Abram T, Babchenko A, Nitzan M, Davidson EM: Pulse oximeter perfusion index as an early indicator of sympathectomy after epidural anesthesia. *Acta Anaesthesiol Scand* 53:1018–1026, 2009.
16. Howell MD, Donnino M, Clardy P, Talmor D, Shapiro NI: Occult hypoperfusion and mortality in patients with suspected infection. *Intensive Care Med* 33:1892–1899, 2007.
17. Dugas AF, Mackenhauer J, Salciccioli JD, Cocchi MN, Gautam S, Donnino MW: Prevalence and characteristics of nonlactate and lactate expressors in septic shock. *J Crit Care* 27:344–350, 2012.
18. Sterling SA, Puskarich MA, Shapiro NI, Trzeciak S, Kline JA, Summers RL, Jones AE: Emergency Medicine Shock Research Network (EMSHOCKNET). Characteristics and outcomes of patients with vasoplegic versus tissue dysoxic septic shock. *Shock* 40:11–14, 2013.
19. Singer AJ, Taylor M, Domingo A, Ghazipura S, Khorasonchi A, Thode HC Jr, Shapiro NI: Diagnostic characteristics of a clinical screening tool in combination with measuring bedside lactate level in emergency department patients with suspected sepsis. *Acad Emerg Med* 21:853–857, 2014.
20. Wira CR, Francis MW, Bhat S, Ehrman R, Conner D, Siegel M: The shock index as a predictor of vasopressor use in emergency department patients with severe sepsis. *West J Emerg Med* 15:60–66, 2014.
21. He H, Liu D, Long Y, Wang X: The peripheral perfusion index and transcutaneous oxygen challenge test are predictive of mortality in septic patients after resuscitation. *Crit Care* 17:R116, 2013.
22. Chung KP, Chang HT, Huang YT, Liao CH, Ho CC, Jerng JS, Yu CJ: Central venous oxygen saturation under non-protocolized resuscitation is not related to survival in severe sepsis or septic shock. *Shock* 38:584–591, 2012.
23. Goldman JM, Petterson MT, Kopotic RJ, et al.: Masimo signal extraction pulse oximetry. *J Clin Monit Comput* 16:475–483, 2000.
24. Galvin EM, Niehof S, Verbrugge SJC, Maissan I, Jahn A, Klein J, van Bommel J: Peripheral flow index is a reliable and early indicator of regional block success. *Anesth Analg* 103:239–243, 2006.

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